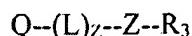


Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

CLAIMS

What is claimed is:

1. (Withdrawn) A method for treating, preventing or inhibiting tumor cell metastasis in a subject comprising administering to the subject in need of such therapy a therapeutically effective amount of an activated $\alpha_{IIb}\beta_3$ receptor antagonist.
2. (Withdrawn) The method of claim 1, wherein the tumor cell metastasis targets an organ system of the subject.
3. (Withdrawn) The method of claim 2, wherein the tumor cell metastasis targets a skeletal system of the subject.
4. (Withdrawn) The method of claim 3, wherein the tumor cell metastasis targets a bone of the subject skeletal system.
5. (Withdrawn) The method of claim 3, wherein the tumor cell metastasis targets a bone cell of the subject skeletal system.
6. (Withdrawn) The method of claim 1, wherein the antagonist is a platelet-specific activated $\alpha_{IIb}\beta_3$ receptor antagonist.
7. (Withdrawn) The method of claim 1, wherein the platelet-specific activated $\alpha_{IIb}\beta_3$ receptor antagonist is a spiro compound.
8. (Withdrawn) The method of claim 7, wherein the spiro compound is represented by the formula:

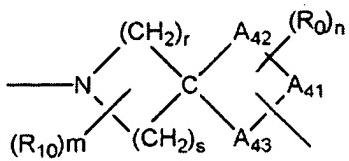


wherein

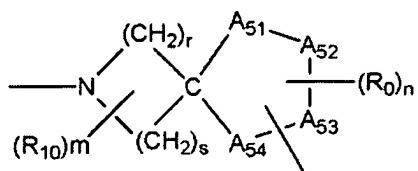
Z is a spirocyclic nucleus selected from the group consisting of Nucleus (A), (B), (C), or (D) represented by the formulas:

Response to Office Action of October 3, 2008
 Application No. 11/564,945 (60005161-0217)

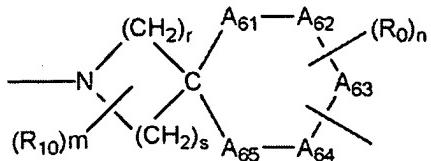
Nucleus (A)



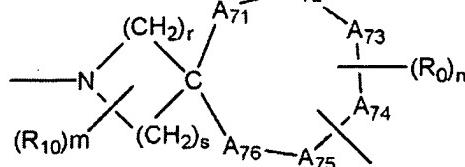
Nucleus (B)



Nucleus (C)



Nucleus (D)



wherein

the group Q--(L)z -- is bound to the nitrogen containing ring of nuclei (A), (B), (C), or (D) and the group R₃ is bound to the ring formed by the groups A₄₁, A₄₂, A₄₃, A₅₁, A₅₂, A₅₃, A₅₄, A₆₁, A₆₂, A₆₃, A₆₄, A₆₅, A₇₁, A₇₂, A₇₃, A₇₄, A₇₅, or A₇₆; or

the group R₃ is bound to the nitrogen containing ring and the group Q--(L)z -- is bound to the ring formed by the groups A₄₁, A₄₂, A₄₃, A₅₁, A₅₂, A₅₃, A₅₄, A₆₁, A₆₂, A₆₃, A₆₄, A₆₅, A₇₁, A₇₂, A₇₃, A₇₄, A₇₅, or A₇₆;

r and s are independently a number from zero to 5 with the proviso that not both r or s are 0 and (r+s) is not more than 6, and z is zero or one;

atoms A₄₁, A₄₂, A₄₃, A₅₁, A₅₂, A₅₃, A₅₄, A₆₁, A₆₂, A₆₃, A₆₄, A₆₅, A₇₁, A₇₂, A₇₃, A₇₄, A₇₅, or A₇₆ are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one of said atoms is carbon;

provided that the hydrogens of the nitrogen containing part of the spirocycle Z may be substituted by a number of m substituents R₁₀, wherein;

m is a number from zero to (r+s); and

R₁₀ is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one or two R₁₀ may be ==O or ==S;

n is a number from zero to 3 in Z of having nuclei (A), or a number from zero to 4 in Z having nuclei (B), a number from zero to 5 in Z having nuclei (C), or a number from zero to 6 in Z having nuclei (D);

R_0 is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one or two R_0 may be ==O or ==S; and

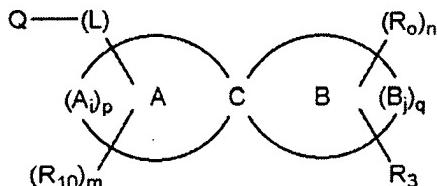
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

Q is a basic group containing one or more basic radicals; and

R_3 is an acidic group containing one or more acid radicals;

or a pharmaceutically acceptable salt, solvate or pro-drug thereof.

9. (Withdrawn) The method of claim 7, wherein the spiro compound is represented by the formula:



wherein

atoms A_i and B_j are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one atom of A_i is carbon, and at least one atom B_j is carbon;

optionally, the rings of the spirobicyclic formed by A_i and B_j , respectively, are partly unsaturated;

p and q are independently numbers from 2 to 6;

m is a number from zero to p;

R_{10} is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one R_{10} may be ==O or ==S, if p is 2 or one or two R_{10} may be ==O or ==S, if p is a number from 3 to 6;

Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

n is the number from zero to q;

R_0 is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one R_0 may be ==O or ==S, if q is 2 or one or two R_0 may be ==O or ==S, if q is a number from 3 to 6;

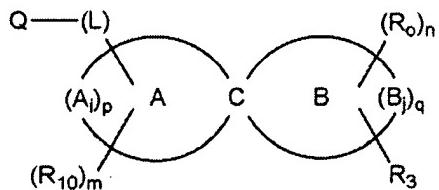
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

Q is a basic group containing one or more basic radicals; and

R_3 is an acidic group containing one or more acid radicals;

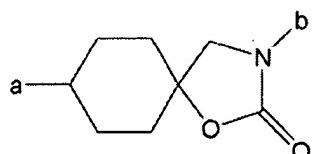
or a pharmaceutically-acceptable salt, solvate or pro-drug thereof..

10. (Withdrawn) The method of claim 7, wherein the spiro compound is represented



by the formula:

wherein



the spirocycle having $(A_i)_p$, C, and $(B_j)_q$ is

m is a number from zero to 9;

R_{10} is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

n is a number from zero to 2;

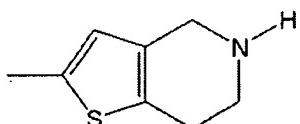
Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

R_0 is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

wherein $Q-(L)$ is attached at a , and R_3 is attached at b ;

--(L)-- is a bond or a substituted or unsubstituted chain selected from the group consisting of CO, CO(C₁-C₆ alkyl), O(C₁-C₆ alkyl), NHCO, and C₁-C₆ alkyl;

Q is a basic group selected from the group consisting of amino, imino, amidino, hydroxyamidino, N-alkylamide, N,N'-dialkylamide, N-arylamide, aminomethyleneamino, aminomethylamino, guanidino, aminoguanidino, alkylamino, dialkylamino, trialkylamino, alkylideneamino, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, indolizinyl, isoindolyl, 3H-indolyl, indolyl, 1H-indazolyl, purinyl, 4H-quinolizinyl, isoquinolyl, quinolyl, phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, amide, thioamide, benzimidino, pteridinyl, 4aH-carbozolyl, carbozolyl, beta-carbolinyl, phenanthridinyl, acridinyl, phenanthrolinyl, phenazinyl, phenarsazinyl, phenothiazinyl, pyrrolinyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, indolinyl, isoindolinyl, quinuclidinyl, morpholinyl, any of the foregoing radicals substituted on a benzene ring, optionally substituted with R_{2c} , wherein R_{2c} is hydrogen or halogen and any of the foregoing radicals substituted by amino, imino, amidino, hydroxyamidino, aminomethyleneamino,



iminomethylamino, guanidino, alkylamino, dialkylamino, trialkylamino, tetrahydroisoquinoline, dihydrosioindole, alkylideneamino or

; and

R_3 is an acidic group selected from the group consisting of CO₂ R₅, (C₁-C₆ alkyl)CO₂ R₅, CO(C₁-C₆ alkyl)CO₂ R₅, CONH(C₁-C₆ alkyl)CO₂ R₅, (C₁-C₆ alkyl)CH(NHR₄)CO₂ R₅, CO(C₁-C₆ alkyl)CH(NHR₄)CO₂ R₅, or CONH(C₁-C₆ alkyl)CH(NHR₄)CO₂ R₅, wherein R₄ is SO₂ (C₁-C₆ alkyl), SO₂ aryl, or SO₂ (substituted aryl); and

R_5 is hydrogen, C₁-C₆ alkyl, aryl, or substituted aryl;

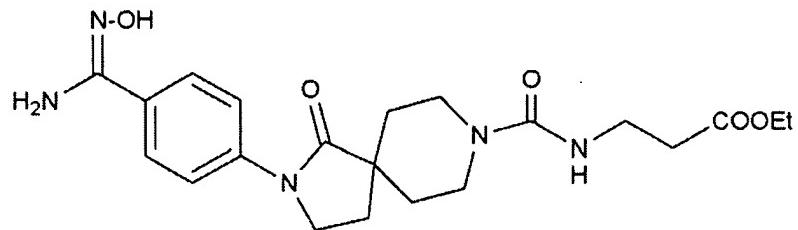
or a pharmaceutically acceptable salt, solvate or pro-drug thereof.

11. (Withdrawn) The method of claim 7, wherein the spiro compound is represented by the formula:



or a pro-drug thereof.

12. (Withdrawn) The method of claim 11, wherein the pro-drug is represented by the formula:



13. (Currently amended) A method for preventing or inhibiting tumor cell growth in a subject comprising administering to the subject in need of such therapy a therapeutically effective amount of an activated $\alpha_{IIb}\beta_3$ receptor antagonist.

14. (Currently amended) The method of claim 13, wherein the tumor cell is comprised by contained within an organ system of the subject.

15. (Currently amended) The method of claim 14, wherein the tumor cell is comprised by contained within a skeletal system of the subject.

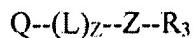
16. (Currently amended) The method of claim 15, wherein the tumor cell is comprised by contained within a bone of the subject skeletal system.

17. (Canceled)

18. (Original) The method of claim 13, wherein the antagonist is a platelet-specific activated $\alpha_{IIb}\beta_3$ receptor antagonist.

19. (Original) The method of claim 18, wherein the platelet-specific activated $\alpha_{IIb}\beta_3$ receptor antagonist is a spiro compound.

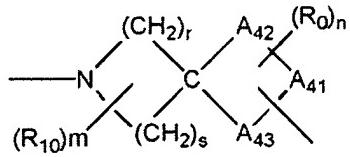
20. (Original) The method of claim 19, wherein the spiro compound is represented by the formula:



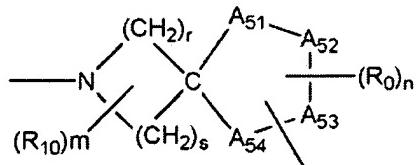
wherein

Z is a spirocyclic nucleus selected from the group consisting of Nucleus (A), (B), (C), or (D) represented by the formulas:

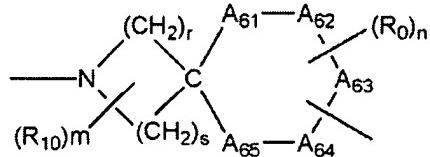
Nucleus (A)



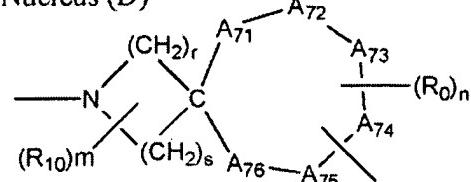
Nucleus (B)



Nucleus (C)



Nucleus (D)



wherein

the group $Q--(L)_Z--$ is bound to the nitrogen containing ring of nuclei (A), (B), (C), or (D) and the group R_3 is bound to the ring formed by the groups $A_{41}, A_{42}, A_{43}, A_{51}, A_{52}, A_{53}, A_{54}, A_{61}, A_{62}, A_{63}, A_{64}, A_{65}, A_{71}, A_{72}, A_{73}, A_{74}, A_{75}$, or A_{76} ; or

Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

the group R_3 is bound to the nitrogen containing ring and the group $Q-(L)Z$ -- is bound to the ring formed by the groups $A_{41}, A_{42}, A_{43}, A_{51}, A_{52}, A_{53}, A_{54}, A_{61}, A_{62}, A_{63}, A_{64}, A_{65}, A_{71}, A_{72}, A_{73}, A_{74}, A_{75}$, or A_{76} ;

r and s are independently a number from zero to 5 with the proviso that not both r or s are 0 and $(r+s)$ is not more than 6, and z is zero or one;

atoms $A_{41}, A_{42}, A_{43}, A_{51}, A_{52}, A_{53}, A_{54}, A_{61}, A_{62}, A_{63}, A_{64}, A_{65}, A_{71}, A_{72}, A_{73}, A_{74}, A_{75}$, or A_{76} are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one of said atoms is carbon;

the hydrogens of the nitrogen containing part of the spirocycle Z may be substituted by a number of m substituents R_{10} , wherein;

m is a number from zero to $(r+s)$; and

R_{10} is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one or two R_{10} may be ==O or ==S;

n is a number from zero to 3 in Z of having nuclei (A), or a number from zero to 4 in Z having nuclei (B), a number from zero to 5 in Z having nuclei (C), or a number from zero to 6 in Z having nuclei (D);

R_0 is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one or two R_0 may be ==O or ==S; and

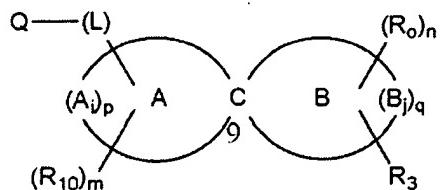
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

Q is a basic group containing one or more basic radicals; and

R_3 is an acidic group containing one or more acid radicals;

or a pharmaceutically-acceptable salt, solvate or pro-drug thereof.

21. (Original) The method of claim 19, wherein the spiro compound is represented by the formula:



Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

wherein

atoms A_i and B_j are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one atom of A_i is carbon, and at least one atom B_j is carbon;

optionally, the rings of the spirobicycle formed by A_i and B_j, respectively, are partly unsaturated;

p and q are independently numbers from 2 to 6;

m is a number from zero to p;

R₁₀ is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one R₁₀ may be ==O or ==S, if p is 2 or one or two R₁₀ may be ==O or ==S, if p is a number from 3 to 6;

n is the number from zero to q;

R₀ is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one R₀ may be ==O or ==S, if q is 2 or one or two R₀ may be ==O or ==S, if q is a number from 3 to 6;

--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

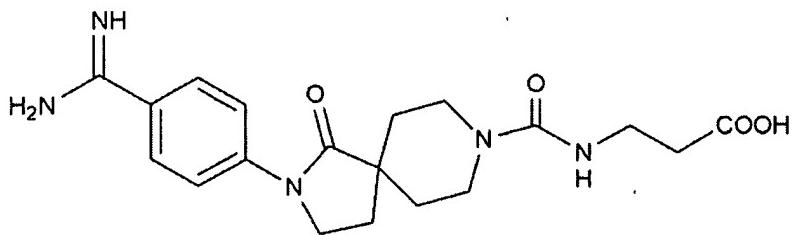
Q is a basic group containing one or more basic radicals; and

R₃ is an acidic group containing one or more acid radicals;

or a pharmaceutically-acceptable salt, solvate or pro-drug thereof.

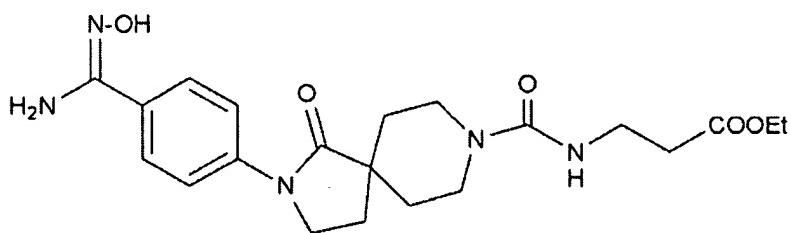
22. (Canceled)

23. (Previously presented) The method of claim 19, wherein the spiro compound is represented by the formula:



or a pro-drug thereof.

24. (Previously presented) The method of claim 19, wherein the spiro compound is represented by the formula:



25. (Withdrawn) A method for destroying a tumor in a subject comprising administering to the subject in need of such therapy a therapeutically effective amount of an activated $\alpha_{1b}\beta_3$ receptor antagonist.

26. (Withdrawn) The method of claim 25, wherein the tumor cell resides in an organ system of the subject.

27. (Withdrawn) The method of claim 26, wherein the tumor cell resides in a skeletal system of the subject.

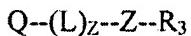
28. (Withdrawn) The method of claim 27, wherein the tumor cell resides in a bone of the subject skeletal system.

29. (Withdrawn) The method of claim 27, wherein the tumor cell resides in a bone cell of the subject skeletal system.

30. (Withdrawn) The method of claim 25, wherein the antagonist is a platelet-specific activated $\alpha_{IIb}\beta_3$ receptor antagonist.

31. (Withdrawn) The method of claim 30, wherein the platelet-specific activated $\alpha_{IIb}\beta_3$ receptor antagonist is a spiro compound.

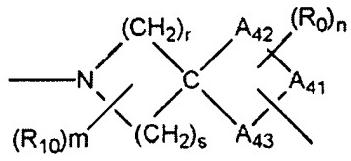
32. (Withdrawn) The method of claim 31, wherein the spiro compound is represented by the formula:



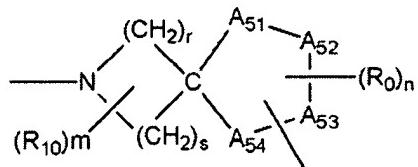
wherein

Z is a spirocyclic nucleus selected from the group consisting of Nucleus (A), (B), (C), or (D) represented by the formulas:

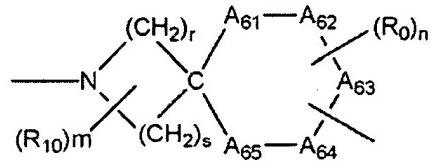
Nucleus (A)



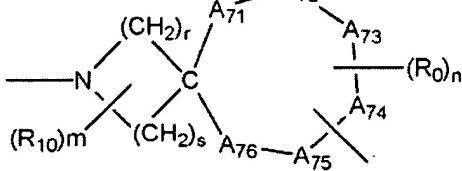
Nucleus (B)



Nucleus (C)



Nucleus (D)



wherein

the group Q--(L)_Z-- is bound to the nitrogen containing ring of nuclei (A), (B), (C), or (D) and the group R₃ is bound to the ring formed by the groups A₄₁, A₄₂, A₄₃, A₅₁, A₅₂, A₅₃, A₅₄, A₆₁, A₆₂, A₆₃, A₆₄, A₆₅, A₇₁, A₇₂, A₇₃, A₇₄, A₇₅, or A₇₆; or

the group R₃ is bound to the nitrogen containing ring and the group Q--(L)_Z-- is bound to the ring formed by the groups A₄₁, A₄₂, A₄₃, A₅₁, A₅₂, A₅₃, A₅₄, A₆₁, A₆₂, A₆₃, A₆₄, A₆₅, A₇₁, A₇₂, A₇₃, A₇₄, A₇₅, or A₇₆;

Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

r and s are independently a number from zero to 5 with the proviso that not both r or s are 0 and (r+s) is not more than 6, and z is zero or one;

atoms A₄₁, A₄₂, A₄₃, A₅₁, A₅₂, A₅₃, A₅₄, A₆₁, A₆₂, A₆₃, A₆₄, A₆₅, A₇₁, A₇₂, A₇₃, A₇₄, A₇₅, or A₇₆ are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one of said atoms is carbon;

the hydrogens of the nitrogen containing part of the spirocycle Z may be substituted by a number of m substituents R₁₀, wherein;

m is a number from zero to (r+s); and

R₁₀ is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one or two R₁₀ may be ==O or ==S;

n is a number from zero to 3 in Z of having nuclei (A), or a number from zero to 4 in Z having nuclei (B), a number from zero to 5 in Z having nuclei (C), or a number from zero to 6 in Z having nuclei (D);

R₀ is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one or two R₀ may be ==O or ==S; and

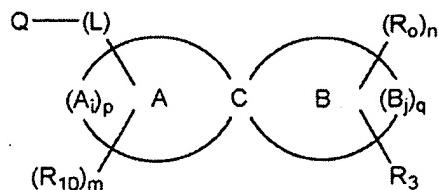
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

Q is a basic group containing one or more basic radicals; and

R₃ is an acidic group containing one or more acid radicals;

or a pharmaceutically-acceptable salt, solvate or pro-drug thereof.

33. (Withdrawn) The method of claim 31, wherein the spiro compound is



Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

represented by the formula:

wherein

atoms A_i and B_j are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one atom of A_i is carbon, and at least one atom B_j is carbon;

optionally, the rings of the spirobicycle formed by A_i and B_j , respectively, are partly unsaturated;

p and q are independently numbers from 2 to 6;

m is a number from zero to p ;

R_{10} is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one R_{10} may be ==O or ==S, if p is 2 or one or two R_{10} may be ==O or ==S, if p is a number from 3 to 6;

n is the number from zero to q ;

R_0 is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one R_0 may be ==O or ==S, if q is 2 or one or two R_0 may be ==O or ==S, if q is a number from 3 to 6;

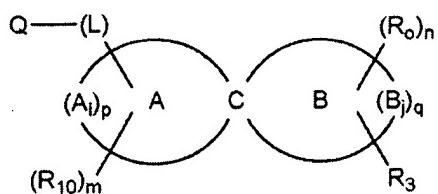
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

Q is a basic group containing one or more basic radicals; and

R_3 is an acidic group containing one or more acid radicals;

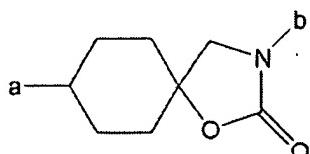
or a pharmaceutically-acceptable salt, solvate or pro-drug thereof..

34. (Withdrawn) The method of claim 31, wherein the spiro compound is



represented by the formula:

wherein



the spirocycle having $(A_i)_p$, C, and $(B_j)_q$ is

m is a number from zero to 9;

R_{10} is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

n is a number from zero to 2;

R_0 is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

wherein $Q-(L)$ is attached at a, and R_3 is attached at b;

--(L)-- is a bond or a substituted or unsubstituted chain selected from the group consisting of CO, CO(C₁-C₆ alkyl), O(C₁-C₆ alkyl), NHCO, and C₁-C₆ alkyl;

Q is a basic group selected from the group consisting of amino, imino, amidino, hydroxyamidino, N-alkylamidine, N,N'-dialkylamidine, N-arylamidine, aminomethyleneamino, aminomethylamino, guanidino, aminoguanidino, alkylamino, dialkylamino, trialkylamino, alkylideneamino, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, indolizinyl, isoindolyl, 3H-indolyl, indolyl, 1H-indazolyl, purinyl, 4H-quinolizinyl, isoquinolyl, quinolyl, phthalazinyl, naphthyridinyl, quinoxaliny, quinazolinyl, cinnolinyl, amide, thioamide, benzamidino, pteridinyl, 4aH-carbozolyl, carbozolyl, beta-carbolinyl, phenanthridinyl, acridinyl, phenanthrolinyl, phenazinyl, phenarsazinyl, phenothiazinyl, pyrrolinyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, indolinyl, isoindolinyl, quinuclidinyl, morpholinyl, any of the foregoing radicals substituted on a benzene ring, optionally substituted with R_{2c} , wherein R_{2c} is hydrogen or halogen and any of the foregoing radicals substituted by amino, imino, amidino, hydroxyamidino, aminomethyleneamino,

Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

iminomethylamino, guanidino, alkylamino, dialkylamino, trialkylamino, tetrahydroisoquinoline, dihydrosioindole, alkylideneamino or

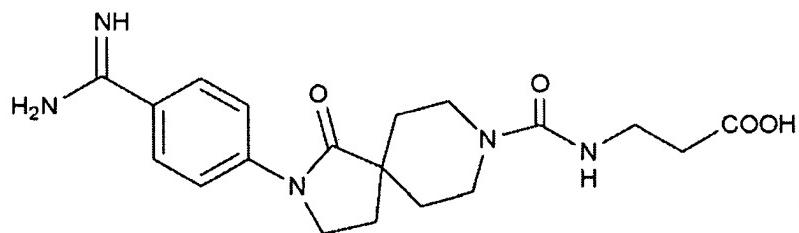
; and

R₃ is an acidic group selected from the group consisting of CO₂ R₅, (C₁-C₆ alkyl)CO₂ R₅, CO(C₁-C₆ alkyl)CO₂ R₅, CONH(C₁-C₆ alkyl)CO₂ R₅, (C₁-C₆ alkyl)CH(NHR₄)CO₂ R₅, CO(C₁-C₆ alkyl)CH(NHR₄)CO₂ R₅, or CONH(C₁-C₆ alkyl)CH(NHR₄)CO₂ R₅, wherein R₄ is SO₂ (C₁-C₆ alkyl), SO₂ aryl, or SO₂ (substituted aryl); and

R₅ is hydrogen, C₁-C₆ alkyl, aryl, or substituted aryl;

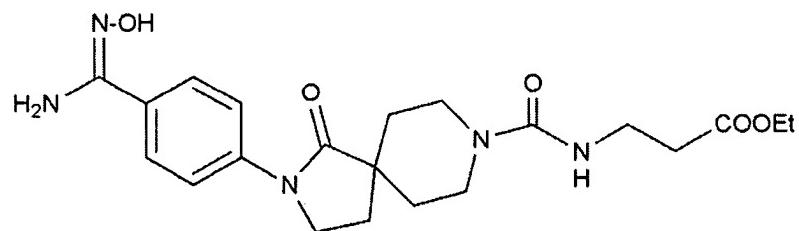
or a pharmaceutically-acceptable salt, solvate or pro-drug thereof.

35. (Withdrawn) The method of claim 31, wherein the spiro compound is represented by the formula:



or a pro-drug thereof.

36. (Withdrawn) The method of claim 35, wherein the pro-drug is represented by the formula:



37. (Withdrawn) A method for treating, preventing or inhibiting tumor cell metastasis to bone in a subject comprising replacing substantially all bone marrow affected by

Response to Office Action of October 3, 2008
Application No. 11/564,945 (60005161-0217)

tumor cell metastasis transplant in the subject, wherein said bone marrow is replaced with β_3 bone marrow.

38. (Withdrawn) A method for treating, preventing or reversing tumor metastasis or formation comprising modulating β_3 integrin expression.

39. (Withdrawn) The method of claim 38, wherein the modulating β_3 integrin expression comprises decreasing the β_3 integrin expression in a mammalian cell.

40. (Withdrawn) The method of claim 39, wherein decreasing the expression comprises transforming the cell to express a polynucleotide anti-sense to at least a portion of an endogenous polynucleotide encoding β_3 integrin.

41. (Withdrawn) The method of claim 39, wherein decreasing the expression comprises transfecting the cell with a polynucleotide anti-sense to at least a portion of an endogenous polynucleotide encoding β_3 integrin.

42. (Withdrawn) The method of claim 39, wherein decreasing the expression comprises transfecting a cell with a siRNA targeting at least a portion of an endogenous polynucleotide encoding β integrin.